

REMARKS

I. Preliminary Remarks

The present invention relates generally to immunotherapy methods providing reduced risk of anaphylaxis. In particular, the invention is directed to the preparation of improved compositions of contiguous overlapping peptide fragments (COPs) for selected allergens wherein the fragments are capable of inducing a T cell response in patients who are hypersensitive to the allergen but wherein administration of the compositions of the invention results in reduced levels of IgE stimulation activity.

According to this method, COPs are generated by the steps of: (1) determining candidate sets of contiguous overlapping peptides by a method comprising: (a) conducting a structural analysis of the selected allergen; (b) selecting one or more separation sites to provide sets of contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; (2) producing said sets of candidate contiguous overlapping peptide fragments; and (3) screening said sets of candidate COPs by the steps of: (a) selecting sets of COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum; and (b) selecting sets of COPs characterized by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum.

II. Outstanding Rejections

Claims 55-61 and 63 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Spertini WO 01/88085 in view of Von Garnier et al. (Eur. J. Immunol., 30:1638-1645), Astori et al. (J. Immunol., 165:3497-3505), Fellrath et al. (J. Allergy Clin. Immunol., 111:854-861), Kammerer et al. (J. Allergy Clin. Immunol., 100(1):96-103 (1997)), and Kammerer et al. (Clin. Exper. Allergy, 27:1016-1026 (1997)).

Claims 55 and 61-62 stand rejected under 35 U.S.C. §103(a) over Spertini WO 01/88085 in view of Von Garnier et al. (Eur. J. Immunol., 30:1638-1645), Astori et al. (J. Immunol., 165:3497-3505), Fellrath et al. (J. Allergy Clin. Immunol., 111:854-861), Kammerer et al. (J. Allergy Clin. Immunol., 100(1):96-103 (1997)), and Kammerer et al.

(*Clin. Exper. Allergy*, 27:1016-1026 (1997)) and in further view of Shanti et al. (*The Journal of Immunology*, 151(10), 5354-5363 (1993)).

Claims 55, 63 and 65 stand rejected under 35 U.S.C. §103(a) over Spertini WO 01/88085 in view of Von Garnier et al., (*Eur. J. Immunol.*, 30:1638-1645), Astori et al. (*J. Immunol.*, 165:3497-3505), Fellrath et al. (*J. Allergy Clin. Immunol.*, 111:854-861), Kammerer et al. (*J. Allergy Clin. Immunol.*, 100(1):96-103 (1997)), and Kammerer et al. (*Clin. Exper. Allergy*, 27:1016-1026 (1997)) and in further view of Spertini et al. (Abstract AAAI presented at AAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in *J. Allergy Clin. Immunol.*, 105(1- pt. 2):S278).

III. Patentability Arguments

- A. The Rejections of Claims 55-61 and 63 Under 35 USC §103(a) as being Unpatentable over Spertini WO 01/88085 in combination with Von Garnier, Astori, Fellrath, Kammerer, and Kammerer should be withdrawn.

Spertini, WO 01/88085 discloses some of the individual elements of independent claim 55 but fails to disclose their combination in the order and manner of the invention to yield an improved method for generating sets of contiguous overlapping peptides (COPs). Similarly, each of the secondary references Von Garnier, Astori, Fellrath, the two Kammerer references, disclose a composition comprising a single set of overlapping peptides which are each used for allergen immunotherapy against various allergens.

Just as Spertini fails to disclose “sets of COPs” so do each of the secondary references every one of which only discloses “a set [of overlapping peptides].” Thus, the cited references show COPs which have been empirically identified but do not disclose a systematic method for identifying such COPs much less the element of “selecting separation sites” to produce sets of COP’s presenting “potential T-cell epitopes but not alpha helix and beta-sheet structural motifs...” as claimed. As discussed previously, the fact that WO 01/88085 states only that the administration of its Api m 6 proteins, peptides or variants “may result in lower levels of IgE stimulation.” (page 19, lines 25-26, emphasis supplied) indicates a hit or miss quality to the prior art method which does not disclose the claimed element of affirmatively selecting separation sites whereby lower levels of IgE would be obtained.

Finally, because Spertini and each of the secondary references only disclose “a [single] set [of overlapping peptides]” they cannot possibly disclose testing multiple sets of COPs or the screening and selecting of multiple sets of COPs having a greater than minimum T cell stimulating activity and a less than a selected maximum of IgE binding activity. For these reasons the rejection of claims 55-61 and 63 should be withdrawn.

- B. The Rejections of Claims 55 and 61-62 under 35 U.S.C. §103(a) over Spertini WO 01/88085 in view of Von Garnier et al., Astori et al., Fellrath et al., Kammerer et al., and Kammerer et al. and in further view of Shanti et al., should be withdrawn.

The rejection of claims 55 and 61-62 under 35 U.S.C. 103(a) as being unpatentable over Spertini, Von Garnier, Astori, Fellrath, the Kammerer references and in view of Shanti et al. (*The Journal of Immunology*, 151(10), 5354-5363 (1993)) should be withdrawn because Shanti discloses dot blotting but fails to make up for the deficiencies of Spertini and the remaining primary references with respect to independent claim 55 as described above.

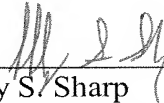
- C. The Rejections of Claims 55, 63 and 65 Under 35 USC §103(a) in view of Spertini et al. in view of Von Garnier et al., Astori et al., Fellrath et al., Kammerer et al., and Kammerer et al. and in further view of Spertini C23 Should Be Withdrawn.

The rejection of claims 55, 63 and 65 under 35 U.S.C. 103(a) as being unpatentable over Spertini, Garnier, Astori, Fellrath, the Kammerer references and in view of in view of Spertini et al. (Abstract AAAI presented at AAAAI (Am. Acad. Allergy Asthma and Immunol.) San Diego, March 3-8, 2000, and published in *J. Allergy Clin. Immunol.*, 105(1-pt. 2):S278) should be withdrawn because Spertini which discloses intradermal skin testes neither makes up for the deficiencies of WO 01/88085 with respect to the elements of independent claim 55 from which dependent claims 63 and 65 depend.

For the foregoing reasons, it is submitted that each of claims 55-63 and 65 should now be allowed. Should the Examiner wish to discuss any issues of form or substance, she is invited to contact the undersigned attorney at the number below.

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Respectfully submitted,

By 
Jeffrey S. Sharp

Registration No.: 31,879
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive
6300 Willis Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant